Division of Comparative Medicine

The Division of Comparative Medicine (DCM) provides animal husbandry and clinical care for all research animals on the MIT campus. Since its inception in 1974, DCM has evolved into a comprehensive laboratory animal program that provides a full range of veterinary and surgical support. Additionally, DCM has had a National Institutes of Health (NIH) grant for training veterinarians for careers in biomedical research for the past 27 years. The division also has an active research program funded by numerous grants from NIH. DCM now has 180 personnel. The division's administrative headquarters and its diagnostic and research laboratories are located on the eighth floor of Buildings 16 and 56. The division now encompasses approximately 193,000 gross square feet in seven buildings devoted to animal research activities on the MIT campus. Replacement of all cage washers and autoclaves in the Building 68 animal facility has commenced as part of a $3 million project funded by the Institute and NIH.

Facility Management and Animal Care

DCM has updated the Laboratory Animals Users' Handbook, and the sixth edition is now available online. The average daily census of laboratory animals increased nearly 3% in FY2015. Mice remain the primary species used by MIT investigators and represent more than 98% of DCM's animal population. The division has two core facilities to support transgenic and gene "knockout" in vivo experiments and performs a range of transgenic services, including in vivo embryo transfer for rederivation of mice with endemic disease that have been imported to MIT from laboratories worldwide, in vitro fertilization, and genotyping of mice. Services now encompass a full range of cryogenic services, including laser-assisted in vitro fertilization and freezing and retrieval of sperm and embryos. The transgenic core also provides genetically engineered mice to the investigative community at MIT. DCM staff provide colony management of mouse models for investigators using mice in their studies. They advise investigators on breeding paradigms and tracking systems to optimize the efficiency of production colonies, as well as providing hands-on services for routine mating, weaning, and genotyping.

DCM also operates two surgery suites, one in Building 46 and the other in E25, along with providing diagnostic laboratory services in support of the veterinary care, surveillance, and quarantine programs. The diagnostic laboratory is equipped and staffed to provide technical services in microbiology, mycology, mycoplasmology, chlamydiology, virology, serology, hematology, parasitology, clinical chemistry, urinalysis, histology, and pathology. Two board-certified veterinary pathologists, Dr. Suresh Muthupalani and Dr. Vasu Bakthavatchalu, provide histopathological interpretations. A pathology diagnostic information system designed to more efficiently manage diagnostic and pathology data acquisition and dissemination was implemented during the past year.

The division had its triennial site visit from the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC International) this past November. We were granted full accreditation for another three years as noted in the follow-up

letter from AAALAC: "The council commends you and the staff for providing and maintaining an exemplary program of animal care and use. Especially noteworthy were the strong institutional commitment to the program, evidenced in part by the numerous renovations, exceptionally talented personnel, and superb animal environments; the highly functional and comprehensive training programs; the outstanding programs of animal husbandry typified by high levels of animal care, knowledgeable personnel, and superior programs of cleaning and sanitation; the notable involvement and oversight by the Committee on Animal Care, demonstrated by thorough protocol and semiannual reviews; the thorough, comprehensive and concise Program Description; and the stellar programs of veterinary care. The Council is pleased to inform you that the program conforms with AAALAC International standards as set forth by the Guide for the Care and Use of Laboratory Animals, NRC 2011. Therefore, FULL ACCREDDITATION shall continue."

Research Activities

In FY2015, DCM faculty and scientific staff had NIH-funded grants (11 in total) supporting a range of studies in areas such as the pathobiology of emerging enterohepatic Helicobacter spp. in mice, the role of Helicobacter pylori as a tumor initiator in gastric cancer, and helicobacter-associated colitis and colon cancer. Other areas of study included the modulation of systemic immune responses and the Th1/Th2 gastric cytokine profile due to H. pylori infection and concurrent infection from parasites, the role of stress-induced reduction in Lactobacillus reuteri in colonic inflammation, and the role of human-derived L. reuteri in activating innate immunity. In addition, division faculty and staff conducted in vivo studies investigating CD4+ and CD25+ regulatory cells' abilities to treat colon and breast cancer, the means by which pathogenic gastrointestinal tract microbes trigger extraintestinal cancers in tissues such as those of the breast, the development of novel techniques for generating gene-deficient animals that can be used across species in a cost-effective manner while decreasing animal usage, and the impact of the microbiome on influenza pathogenesis and immune response. Finally, they investigated differential environmental stabilities of influenza virus particles and the viral ecology, epizootiology, and evolution of influenza in animal and environmental reservoirs. Total research expenditures were $2.7 million in FY2015.

FY2015 was the 27th year of the division's NIH postdoctoral training grant, which is funded through 2018. Our NIH three- to four-year sponsored postdoctoral training program has been completed by 55 trainees; 39 have become diplomates of the American College of Laboratory Animal Medicine. An additional 16 DVMs, PhDs, or MDs completed postdoctoral fellowships sponsored by individual R01 or program project grants. Many former trainees hold leadership positions in academia as well as pharmaceutical and biotechnology companies. Previous fellows have been elected to fill the presidencies of three national organizations: Dr. Steve Niemi (director of animal resources at Harvard University) at the American College of Laboratory Animal Medicine and both Dr. Scott Perkins (director of the Division of Laboratory Animal Medicine at Tufts-New England Medical Center) and Dr. Kim Saunders (professor and director of the Department of Comparative Medicine at Oregon Health and Science University) at the American Association for Laboratory Animal Science. Dr. Susan

Erdman, a former DCM postdoctoral fellow and currently the division's assistant director, is past president of the American Committee on Laboratory Animal Diseases.

The NIH training grant also provides short-term training opportunities for veterinary students interested in careers in comparative medicine. During FY2015, DCM had six short-term trainees for periods ranging from eight to 10 weeks. Many have, upon graduation, entered careers in biomedical research. Sixty-six veterinary students have participated in the summer training program during the past 10 years. Also, the division hosted 12 veterinary students who elected to spend two- to four-week externships at DCM during the school year.

Academic Activities

DCM faculty and staff published 34 peer-reviewed papers during the past year and presented numerous research papers at national and international meetings. The third edition of Laboratory Animal Medicine, edited by Drs. James Fox and Mark Whary, has just been published. DCM staff members wrote 11 chapters for this text.

Dr. Fox continues to serve on the boards of directors of national associations and on editorial boards of scientific journals. He most recently served on the Physician Scientist Workforce Committee commissioned by the director of NIH. Dr. Fox is also a member of the National Academy of Sciences Global Forum on Innovations in Health Professional Education. In addition, he was the recipient of the 2014 Pravin N. Bhatt Excellence in Research Award from the American Association for Laboratory Animal Science. Dr. Whary, associate director of DCM, is a member of the editorial boards of Comparative Medicine and the Journal of the American Association for Laboratory Animal Science. He was recently elected to serve on the council for AAALAC. Dr. Susan Erdman, DCM assistant director and principal research scientist, serves on an ad hoc review committee for NIH. Dr. Suresh Muthupalani, DCM chief of comparative pathology, also serves on an NIH ad hoc review committee.

DCM faculty and staff teach 20.202 In vivo Models: Principles and Practices, a graduate course in the Department of Biological Engineering. Dr. Jonathan Runstadler teaches 20.109 Laboratory Fundamentals in Biological Engineering and 20.450 Molecular and Cellular Pathophysiology. Dr. Robert Marini, assistant director and chief of surgical resources, serves as a lecturer in the Harvard-MIT Division of Health Sciences and Technology, where he is involved in the teaching of two courses (HST 542J Quantitative Systems Physiology and HST090 Cardiovascular Pathophysiology).

Committee on Animal Care Activities

All students, staff, visiting scientists, and principal investigators who use animals in teaching or research must be certified by the Committee on Animal Care (CAC). To enable protocol submission and personnel training, CAC's website provides required forms, continuing education materials, and information about CAC activities. In conjunction with CAC, DCM staff have developed an online training program and are using the Collaborative Institutional Training Initiative's online courses via the MIT

Learning Center. These tools are combined with individual orientation and training in animal use by the veterinary staff at the Institute. Individual and group didactic training sessions for Institute personnel on topics pertaining to the care and use of laboratory animals are also offered on a regular basis. CAC, DCM, and MIT Medical coordinate an occupational health program for animal-related occupational health issues. In addition to its work on the MIT campus, CAC provides protocol reviews for the Whitehead Institute for Biomedical Research and the Broad Institute.

James G. Fox
Director
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